Remarks

The Office Action mailed June 29, 2001 has been received and reviewed. Claims 1, 4-15, 17-19, and 28 through 36 are currently pending. Applicants have amended the application as previously set forth. All amendments are made without prejudice or disclaimer. Reconsideration of the referenced application is respectfully requested in light of the amendments and remarks presented herein.

1. Specification

The Examiner objected to the specification as allegedly being full of terms which are not clear, concise and exact. Applicants have reviewed the specification and, pursuant to 37 C.F.R. §§ 1.121 and 1.125 (as amended to date) please enter the substitute specification in clean form and including paragraph numbers **[0001]** through **[0044]** attached hereto as Appendix A. A marked-up substitute specification to clearly identify amendments to the specification as required by 37 C.F.R. § 1.121(b)(3)(iii) is attached hereto as Appendix B. Reconsideration and withdrawal of the objection is requested.

2. 35 U.S.C. §112

Claims 1, 4-15 and 28 through 36 were rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject mater which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleged that the applicants have not disclosed any glucocorticoid other than dexamethasone.

Applicants respectfully submit that independent claim 1 as filed, from which claims 4-15 and 28 through 36 depend, included the limitation, "a glucocorticoid hormone". Written description requirement issues most often come "into play where claims not presented in the application when filed are presented thereafter." *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1114 (CAFC 1991). Applicants respectfully submit that glucocorticoids are a well known class of adrenocorticotropic hormones. (*See, for example*, Goodman and Gilman's The Pharmacological Basis of Therapeutics, Goodman Gilman, A et al. (Seventh Ed.) Chapter 23 Adrenocorticotrophic Hormone: Adrenocortical Steroids and their Synthetic Analogs; Inhibitors of Adrenocortical Steroid Biosynthesis, pp. 1459-

1489; Remington's Pharmaceutical Sciences, Chase et al. (Sixteenth Ed.) Adrenal Hormones pp. 898-912). Glucocorticoids are discussed generally as a class with respect to physiology, biological activity, side effects, drug interactions, absorption, fate and excretion, and therapeutic uses. (Remington's, pages 898-901). Thus, because of such uniformity within the class of glucocorticoids, applicants respectfully submit that one of skill in the art would understand that dexamethasone is merely an exemplary glucocorticoid and that the disclosure is applicable to all glucocorticoids. Reconsideration and withdrawal of the rejection is respectfully requested.

Further, the Examiner argued that the specification, while being enabled for the in vitro induction of non-responsiveness of MHC-matched clonal T cells to a defined antigen when dexamethasone-treated dendritic cells have been loaded with the same defined antigen, does not provide enablement for in vivo or in vitro induction of non-responsiveness of polyclonal T cells to any defined antigen or the in vivo induction of non-responsiveness when an "unwanted T-cell response" is ongoing. The Examiner cites Tisch as disclosing that the administration of antigen after pathogenic T cells have been activated may have an exacerbating effect on the disease, rather than a tolerogenic one. (Office Action, page 5). Tisch discloses treating autoimmune disease by targeting autoreactive T cells. (Tisch, page 437, col. 1). Tisch suggests inducing tolerance by using an autoantigen. (Id.) Tisch acknowledges that problems can occur with this method depending on the particular antigen used to induce tolerance.

The present invention acknowledges that activated T cells have been considered primary targets to treat certain conditions. (Specification, page 2, lines 3-7). However, the present invention discloses targeting dendritic cell activation by transforming an alternative activation pathway. (Id. at page 2, lines 27-36). The present invention provides,

> DC activation through engagement of CD40-CD40L is a key stipulatory event for the generation of effective Th1 and CD4-dependent CTL responses in vivo. This pathway however is involved in the development of unwanted T cell responses leading to the autoimmune disease or organ-transplant rejection. Until now, treatment of patients suffering from such disorders largely relied on the systemic administration of GC hormones. This treatment does not only suppress pathogenic T cell responses, but also induces a general state of immunosupresssion and metabolic and endocrine side effects. The present invention demonstrates that activation of human monocyte-derived DC through CD40, in the presence of GC such as DEX, results in an IL-10-producing APC that is a poor simulator for Th1-type responses that can even confer hyporesponsiveness to Th1 cells. The present invention therefore indicates that such DC loaded with appropriate antigens can be

exploited as a novel approach for specifically downregulating unwanted T cell responses in vivo.

(Id., page 4, lines 1-20)(citations omitted).

Thus, the present invention shows that GC, such as DEX, convert CD40 ligation on human monocyte-derived DC and is transformed into an alternate pathway. DEX profoundly affects the CD40-dependent maturation of human monocyte-derived DC, not only by preventing the upregulation of costimulatory adhesion and MHC surface molecules, but also by causing these cells to secrete the anti-inflammatory mediator IL-10 instead of the Th1 stimulatory cytokine IL-12. (Id., page 2, lines 27-36). Applicants respectfully submit that the present invention is directed toward a different class of DC and the activation of DC along an alternative pathway creates a different immune response. (Id., page 4, lines 24-31). Thus, when the DC of the present invention present antigen, an alternate immune response is already underway and, therefore, the concerns of Tisch are not applicable to the present invention. Reconsideration and withdrawal of the rejection is requested.

3. 35 U.S.C. §102

Claims 17 through 19 stand rejected under 35 U.S.C. §102(b) as being anticipated by Steptoe et al.

Applicants have amended claim 17 to include the limitation "providing a dendritic cell activated in the presence of a glucocorticoid hormone and capable of functionally modifying said T-cell such that the response of T-cell to said antigen is altered." Applicants respectfully submit that Steptoe fails to teach all of the limitations of claim 17, as amended. Claims 18 and 19 depend from claim 17 and avoid the cited art for the same reasons. Reconsideration and withdrawal of the rejection is requested.

4. Drawings

Accompanying this Amendment is a letter to the Chief Draftsman submitting formal drawings. Acceptance of the formal drawings is respectfully requested.

Conclusion

If questions exist after consideration of the foregoing, the Office is kindly requested to contact applicants' attorney at the number given below.

Respectfully submitted,

Krista Weber Powell
Registration No. 47,867
Attorney for Applicants
TRASKBRITT
P. O. Box 2550
Salt Lake City, Utah 84110-2550
Telephone: (801) 532-1922

Date: October 29, 2001